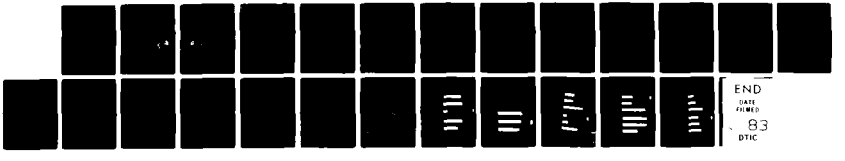
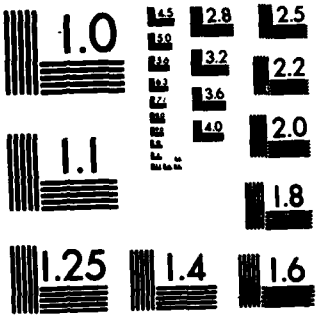
AD-A124 922 MALATHION ADMINISTRATION: EFFECTS ON PHYSIOLOGICAL AND 1/1
PHYSICAL PERFORMANCE IN THE HEAT(U) ARMY RESEARCH INST
OF ENVIRONMENTAL MEDICINE NATICK MA
UNCLASSIFIED R FRANCESCONI ET AL. 09 DEC 82 F/G 6/20 . NL



END
DATE FILMED
83
DTIC



UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER	2. GOVT ACCESSION NO. A124922 / 3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Malathion Administration: Effects on Physiological and Physical Performance in the Heat.	5. TYPE OF REPORT & PERIOD COVERED 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Ralph Francesconi, Roger Hubbard, and Milton Mager	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Research Institute of Environmental Medicine, Natick, MA 01760	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 611102S1000 3E161102BS10 24182101005
11. CONTROLLING OFFICE NAME AND ADDRESS US Army Medical Research and Development Command Ft. Detrick, Frederick, MD 21701	12. REPORT DATE 9 December 1982 13. NUMBER OF PAGES 22
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) Same	15. SECURITY CLASS. (of this report) UNCLASSIFIED 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Distribution of this document is unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

NA

18. SUPPLEMENTARY NOTES

NA

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

NA

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

To determine the effects of low-dosage organophosphate administration on exercise in a hot environment, malathion (7.5 mg/day, 4 days) was administered IP to rats, and effected a 35% ($p < .01$) reduction in plasma cholinesterase levels. Treadmill endurance (9.14m/min, no incline, 36°C ambient) was unaffected when the animals were exercised to hyperthermic exhaustion (Tre ~43°C). While rates of heat gain were similar between groups, malathion-treated rats displayed higher Tsk ($p < .05$) at a number of sampling times during the treadmill run. While creatine phosphokinase levels were unaffected by either cholinesterase

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

inhibition or exercise in the heat, lactate dehydrogenase activities were increased ($p<.01$) in both groups following hyperthermic exhaustion. Although plasma levels of lactate, potassium, urea nitrogen, and creatinine were all significantly ($p<.01$) increased as a result of exercise in the heat, these increments were not excerbated by cholinesterase inhibition. Results generally indicated that at this moderate level of cholinesterase inhibition, malathion administration did not adversely affect physiological, physical, or thermoregulatory efficacy.

Malathion Administration: Effects on Physiological and Physical Performance in the Heat

Ralph Francesconi, Roger Hubbard, and Milton Mager

US Army Research Institute of Environmental Medicine

Natick, MA 01760

Send Proofs To: Ralph Francesconi
Heat Research Division
US Army Research Institute of Enviromental Medicine
Natick, MA 01760

Abstract

To determine the effects of low-dosage organophosphate administration on exercise in a hot environment, malathion (7.5 mg/day, 4 days) was administered IP to rats, and effected a 35% ($p < .01$) reduction in plasma cholinesterase levels. Treadmill endurance (9.14m/min, no incline, 35°C ambient) was unaffected when the animals were exercised to hyperthermic exhaustion (Tre ~43°C). While rates of heat gain were similar between groups, malathion-treated rats displayed higher Tsk ($p < .05$) at a number of sampling times during the treadmill run. While creatine phosphokinase levels were unaffected by either cholinesterase inhibition or exercise in the heat, lactate dehydrogenase activities were increased ($p < .01$) in both groups following hyperthermic exhaustion. Although plasma levels of lactate, potassium, urea nitrogen, and creatinine were all significantly ($p < .01$) increased as a result of exercise in the heat, these increments were not exacerbated by cholinesterase inhibition. Results generally indicated that at this moderate level of cholinesterase inhibition, malathion administration did not adversely affect physiological, physical, or thermoregulatory efficacy.

Key Words: Cholinesterase inhibition; hyperthermic exhaustion; heat injury; clinical chemical indices

Introduction

While the behavioral and mental performance decrements induced by administration of organophosphates to a variety of laboratory animals have been well documented and reviewed (5), very little data have been presented regarding effects on physical performance or thermoregulation. Meeter (22) had reported that organophosphate intoxication usually elicited rapid decreases in rectal temperature of rats caused by increased heat loss via vasodilation in the tail. Ahdaya et al. (1) demonstrated that parathion was effective in reducing rectal temperatures in mice, and that there was a correlation between the degree of cholinesterase inhibition and the magnitude of the temperature decrement. However, no reports were available concerning the effects of organophosphate poisoning on thermoregulatory or physiological responses during exercise in the heat.

This was of particular interest to us since atropine, widely recognized as a very effective antidote for organophosphate poisoning (12,13), has also been reported to affect heat-loss mechanisms (3,7), largely through its anticholinergic action (2,17). In a recent communication (15) we have demonstrated that atropinized rats displayed greatly increased heating rates when passively exposed to a hot environment (41.5°C). We attributed these increments in rectal temperature to the absence of saliva- and urine-spreading behavior in the atropinized rats. However, while we have demonstrated (10) that chronic chlorpromazine administration compromises the ability to work in the heat, the effects of atropine, singly or in combination with organophosphate poisoning, on work in the heat have not been reported.

To approach this problem systematically, we initially wished to investigate the physiological and physical decrements induced by an organophosphate poison

which effected moderate levels of plasma cholinesterase inhibition. Malathion is a commercially available insecticide used extensively as an organophosphate inhibitor of brain, red cell, and plasma cholinesterase activity (24,29). Further, modulation of the dosage level is effective in achieving predetermined levels of cholinesterase inhibition (6,18). Consequently, we could attain a moderate level of cholinesterase inhibition and quantitate its effects on the physical work capacity and thermoregulatory responses of a heat-exposed, exercising rat model.

Methods

Adult, male rats (Charles River Breeding Laboratories) were divided into two groups (n=12/group), one of which served as a control. Rats were held in a windowless room maintained at 22°C ± 1.0°C, one animal per cage, with free access to food (Charles River Laboratory Chow) and water. An automatic timing device controlled fluorescent lighting (on, 0600-1800 h daily) to aid in establishing and standardizing diurnal/nocturnal periodicities of body temperature. No pre-conditioning to heat or exercise was necessary since no adaptational effects were under consideration, and naive animals will readily exercise at the slow treadmill speed selected.

Malathion (95%, technical grade, Analabs, Inc., New Haven, CT) was diluted with a mixture of acetone, 70% ethyl alcohol, physiological saline (1:4.2:6.2) aseptically to achieve a final concentration of 7.5 mg malathion/1.0 ml diluent. One ml (7.5 mg) was thus administered intraperitoneally to the experimental group each day for four consecutive days to attain a total dosage of 30 mg. Prior to the first injection each rat (experimental and control) was fitted with an indwelling catheter inserted permanently into the exterior jugular vein for blood sampling. Upon recovery from this minor surgery and immediately

before the first injection, a 1.0 ml blood sample was taken (control or time 0), the hematocrit measured, and the blood was centrifuged (10000 g, 4°C) and the plasma removed and frozen (-20°C) for subsequent analysis. Control rats were treated identically save for the injection of 1.0 ml diluent only on each of 4 consecutive days.

Approximately 10 min after the final injection a second blood sample was obtained and treated exactly as the first; this was the pre-run blood sample. Before initiating exercise, a rectal probe (model #701, Yellow Spring Instr. Co., Yellow Springs, Ohio) was inserted to a depth of 6 cm, and a surface probe (Yellow Springs #709) was affixed mid-length on the tail. Both probes were securely attached with plastic adhesive tape so as to be unaffected positionally by the subsequent exercise. Rectal (Tre) and tail-skin (Tsk) temperatures were monitored on a minute-by-minute basis during exercise (9.14 m/min, level treadmill) in a hot (35°C, 25% RH) environmental chamber until hyperthermic exhaustion (Tre = 43°C) ensued. Immediately upon completion of the treadmill run a post-run blood sample was removed and treated as the previous, and the rats were then returned to the holding room.

In addition to assaying all plasma samples for the commonly reported indices of heat/exercise injury (14,16), each sample was also analyzed for cholinesterase activity to determine the efficacy of malathion inhibition. Cholinesterase levels were quantitated using kits supplied by Sigma Chemical Co. (St. Louis, MO) after procedures described in their technical bulletin (#420). Glucose was quantitated using Worthington Statzyme test kits while plasma lactates were measured by means of Sigma test kits, each according to standard procedures outlined in the respective technical bulletins. Potassium (K^+) and sodium (Na^+) levels were analyzed by flame photometry (Radiometer, Copenhagen). Creatine phosphokinase (CPK), lactic acid dehydrogenase (LDH),

urea nitrogen (UN), and creatinine levels were estimated using Worthington test kits by methods described in the appropriate technical bulletins. Spectrophotometric procedures were carried out on a Gilford Stasar III automated spectrophotometer.

Statistical analyses were made by analysis of variance (21) followed by Tukey's t test (20) for all-pair comparisons; the paired and non-paired t test were also used where appropriate. The null hypothesis was rejected at $p < 0.05$.

Results

Fig. 1 demonstrates the effects of malathion administration on the rectal and tail-skin temperature responses to exercise in the heat to hyperthermic exhaustion. The results did not indicate that Tre was affected by malathion administration; the slight divergence noted near the end of the run arose from the inability of several rats to continue beyond 35 min. However, Tsk was elevated by as much as 1.3°C in the malathion-treated group. Despite virtually identical starting Tsk ($\bar{X}$ = 23.06°C, control; $\bar{X}$ = 23.00°C, malathion), Tsk was statistically significantly ($p < .05$, minimally) elevated from 10-22 min of exercise, in the malathion-treated group. The mean endurance capacity was identical for both groups ($\bar{X}$ = 37.0 min, control; $\bar{X}$ = 37.06 min, malathion), thus totally unaffected by this dosage level of malathion. Fig. 2 demonstrates that average weight (water) loss during exercise in the heat was not different ($p > .05$) between groups ($\bar{X}$ = 9.06 g, control; $\bar{X}$ = 8.0 g, malathion). Hematocrit ratios were unaffected ($p > .05$) by pretreatment with malathion; the hemodilution observed in the post-exercise samples ($p < .02$, control; $p < .001$, malathion) might be partially attributable to the initial blood withdrawal although under similar conditions, we have observed hemodilution even when much smaller volumes (0.3 ml) have been taken.

That malathion administration achieved a significant inhibition of plasma cholinesterase is depicted in Fig. 3. In the first (control, malathion) plasma sample of the group to be treated with malathion, the mean specific activity of cholinesterase was 25.47 $\pm$ 1.70 ($\bar{X} \pm$ S.E.x) umoles of acetate formed per hour per ml of plasma. After 4 consecutive days of malathion administration this activity declined significantly to 16.48 $\pm$ 1.42 ($p < .01$), an inhibition of 35.4%. It is also of interest to note that exercise in the heat to hyperthermic exhaustion (pre vs post samples both groups) had no effect ($p > .05$) on plasma cholinesterase levels.

In Fig. 4 the effects of malathion administration and exercise in the heat to hyperthermic exhaustion on circulating levels of CPK and LDH are illustrated. Initially, it should be noted that CPK levels are rather inconsistent between groups. Several rats in the malathion treated group had CPK levels greater than 300 U, thus contributing to the high mean level of activity in the control sample. The reasons for this elevated activity were not obvious, but activity had returned to normal levels immediately prior to exercise in the heat. The relatively brief period of treadmill exercise is evidently insufficient to induce consistently elevated levels in the post-run samples. Alternatively, LDH levels, while unaffected ($p > .05$) by malathion treatment, demonstrate significant ($p < .01$, both groups) increments as a result of exercise in the heat to hyperthermic exhaustion. Analogous results are illustrated in Fig. 5 for circulating levels of lactate, i.e. no effects of malathion administration while heat/exercise injury induces significant ($p < .01$) increments in both groups. Also depicted in Fig. 5 are the effects of malathion administration and exercise in the heat to hyperthermic exhaustion on plasma glucose levels. However, neither condition affected ($p > .05$) circulating glucose levels.

by either treatment. Finally, while malathion administration had no effects ($p > .05$) on circulating urea nitrogen and creatinine levels, both indices of clinical heat injury were elevated significantly ($p < .01$) by exercise in the heat.

Discussion

Generally, the results of the present investigation demonstrated that malathion administration, at a dosage level sufficient to induce moderate inhibition of circulating cholinesterase levels, had no debilitating effects on physical performance in a hot environment. By contrast, Kurtz (18), using Sprague-Dawley rats, had reported that mental performance was affected 1 hour after injection of malathion although blood and brain cholinesterases remained at 90% of control levels. Thus, while mental performance appears to be greatly affected by organophosphate intoxication (5,19), there are a number of reports indicating that a variety of physiological factors may be more resistant. For example, Chakraborty et al. (4) demonstrated in rats that neither malathion nor the more potent insecticide, parathion, had effects on hemoglobin concentration or kidney and liver organ weight to body weight ratios. Paul et al. (26) reported that an oral dose of 100 mg/kg malathion to rats induced no respiratory distress symptomatology. Villeneuve et al. (30) reported, also in rats, that consumption of up to 5 ppm parathion in food for 42 days had no significant effects on the organ to body weight ratios of heart, brain, liver, kidney, spleen or thymus, although body weights were reduced. Since the LD50 of orally administered malathion is in the order of 340 mg/kg (26), it may not be surprising that an intraperitoneal dosage of approximately 100 mg/kg over 4 experimental days did not affect physical work capacity.

While Meeter and Wolthuis (23) demonstrated generalized hypothermia as a result of administration of organophosphate anticholinesterases, they also reported that increasing the ambient temperature reduced the magnitude of this hypothermic response. Meeter (22) later showed that greater heat loss through the tail may be responsible for the generalized hypothermia. In the present experiments the initial Tre and Tsk between groups are essentially identical, and indicate no chronic effects on thermoregulation of repeated low-dosage malathion administration. The increased Tsk during exercise in the heat in the malathion-treated rats is of statistical significance and may be related to the original observation of Meeter (22) concerning increased tail-skin heat loss after pesticide administration. However, this observation appears to be of no physiological importance since heating rates, manifested in increments in Tre during exercise in the heat, are virtually identical between groups.

While the behavioral (5,19) and clinical (8,27) manifestations of organophosphate intoxication have been extensively reported, fewer publications have addressed the clinical chemical alterations subsequent to pesticide exposure. Namba et al. (25) have noted that accidental or deliberate ingestion of pesticides can elicit circulatory hyperglycemia, slightly elevated blood urea nitrogen, and no effects on glutamate-oxaloacetate (GOT) or glutamate-pyruvate (GPT) transaminases. Sidell (28), in reviewing several cases of accidental exposure to much stronger anti-cholinesterases, reported no acute effects on hematocrit, blood urea nitrogen, creatinine, GOT, Na^+ or K^+. Paul et al. (26) also observed marked hyperglycemia as one of the few pathological sequelae to malathion administration. Evidently, the intensity of malathion intoxication achieved in the present investigation was insufficient to induce significant effects on circulating glucose levels. In fact, the incurrence of heat/exercise injury, while producing anticipated increments of the appropriate clinical chemical indices, had no more effect on the malation-treated rats than controls.

We concluded from these studies that organophosphate administration, sufficient to induce moderate cholinesterase inhibition, did not have deleterious effects on endurance in a hot environment. While tail-skin temperature was increased, body heat gain was unaffected in the malathion treated groups. Exercise in the heat to hyperthermic exhaustion caused significant increments in plasma levels of lactate, LDH, K^+, UN, and creatinine, but these effects were not exacerbated by malathion administration. Further experiments are planned to examine the effects of more severe intoxication, in the presence and absence of atropine prophylaxis, on physiological responses to exercise in the heat.

Figure Legend

Fig. 1. Effects of malathion administration and exercise in the heat on the rectal and tail-skin temperatures of rats. Malathion treated rats (n=12) received 7.5 mg malathion/day for 4 consecutive days; controls (n=12) received the diluent only. Rats ran at 9.14m/min, level treadmill at 35°C until hyperthermic exhaustion ensued (Tre = 43°C).

Fig. 2. Effects of malathion administration and exercise in the heat to hyperthermic exhaustion on hematocrit ratios and body weights. The control blood sample was removed before the initial injection of malathion; the pre and post blood samples and body weights were obtained immediately prior and subsequent to exercise in the heat to hyperthermic exhaustion. All remaining conditions are as noted under Fig. 1.

Fig. 3. Effects of malathion administration and exercise in the heat to hyperthermic exhaustion on plasma levels of cholinesterase activity. All conditions are as reported under Figs. 1 and 2.

Fig. 4. Effects of malathion administration and exercise in the heat to hyperthermic exhaustion on plasma levels of creatine phosphokinase and lactic acid dehydrogenase activities. All conditions noted under Figs. 1 and 2.

Fig. 5. Effects of malathion administration and exercise in the heat to hyperthermic exhaustion on plasma levels of lactate and glucose. All conditions noted under Figs. 1 and 2.

Fig. 6. Effects of malathion administration and exercise in the heat to hyperthermic exhaustion on plasma levels of potassium (K^+) and sodium (Na^+). All conditions are as noted under Figs. 1 and 2.

Acknowledgements

The authors gratefully acknowledge the skilled technical assistance of SP-5 Shawn Wright and Natalie Leva. We also thank Sandra Beach, Pat Basinger and Julie Cyphers for typing the manuscript.

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official US Department of the Army position, policy, or decision unless so designated by other official documentation.

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," as prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council.

References

1. Ahdaya, S. M., P. V. Shah, and F. E. Guthrie. Thermoregulation in mice treated with parathion, carbaryl, or DDT. Toxicol. Appl. Pharmacol. 35:575-580, 1976.

2. Batra, G., R. Traystman, H. Rudnick, and H. Menkes. Effects of body position and cholinergic blockade on mechanisms of collateral ventilation. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 50:358-362, 1981.

3. Breslin, F. J., E. R. McFadden, Jr., R. H. Ingram, Jr., and E. C. Deal, Jr. Effects of atropine on respiratory heat loss in asthma. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 48:619-623, 1980.

4. Chakraborty, D., A. Bhattacharyya, K. Majumdar, K. Chatterjee, S. Chatterjee, A. San, and G. C. Chatterjee. Studies on L-ascorbic acid metabolism in rats under chronic toxicity due to organophosphorous insecticides: effects of supplementation of L-ascorbic acid in high doses. J. Nutr. 108:973-980, 1978.

5. Clark, G. Organophosphate insecticides and behavior. A review. Aerosp. Med. 42:735-740, 1971.

6. Cohen, S. D. and M. Ehrich. Cholinesterase and carboxylesterase inhibition by dichlorvos and interactions with malathion and triorthotolyl phosphate. Toxicol. Appl. Pharmacol. 37:39-48, 1976.

7. Craig, F. N. Effects of atropine, work and heat on heart rate and sweat production in man. J. Appl. Physiol. 4:826-833, 1952.

8. Durham, W. F. and W. J. Hayes. Organic phosphorous poisoning and its therapy. Arch. Environ. Hlth. 5:21-47, 1962.

9. Francesconi, R. and M. Mager. Alcohol consumption in rats: effects on work capacity in the heat. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 50:1006-1010, 1981.

10. Francesconi, R. and M. Mager. Chronic chlorpromazine administration in rats: effects on ability to work in the heat. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 50:509-512, 1981.

11. Francesconi, R. and M. Mager. Prostaglandin E_1 hyperthermia: effects on ability to work in the heat. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 51:62-67, 1981.

12. Harris, L. W., D. L. Stitcher, and W. C. Heyl. The effects of pretreatments with carbamates, atropine and mecamylamine on survival and on soman-induced alterations in rat and rabbit brain acetylcholine. Life Sci. 26:1885-1891, 1980.

13. Harris, L. W., D. L. Stitcher, W. C. Heyl, C. N. Lieske, J. R. Lowe, J. H. Clark, and C. A. Broomfield. The effects of atropine-oxime therapy on cholinesterase activity and survival of animals intoxicated with p-nitrophenyl di-n-butylphosphinate. Toxicol. Appl. Pharmacol. 49:23-29, 1979.

14. Hubbard, R., W. Bowers, and M. Mager. A study of physiological, pathological and biochemical changes in rats with heat- and/or work-induced disorders. Israel J. Med. Sci. 12:884-886, 1976.

15. Hubbard, R. W., C. B. Matthew, and R. Francesconi. The heat-stressed rat: effects of atropine, desalivation or restraint. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. In press, 1982.

16. Hubbard, R., W. Matthew, J. Linduska, F. Curtis, W. Bowers, I. Leav, and M. Mager. The laboratory rat as a model for hyperthermic syndromes in humans. Am. J. Physiol. 231:1119-1123, 1976.

17. Jones, R. S. G. Long-term administration of atropine, imipramine, and viloxazine alters responsiveness of rat cortical neurones to acetylcholine. Can. J. Physiol. Pharmacol. 58:531-535 1980.

18. Kurtz, P. J. Dissociated behavioral and cholinesterase decrements following malathion exposure. Toxicol. Appl. Pharmacol. 42:589-594, 1977.

19. Levin, H. S. and R. L. Rodnitzky. Behavioral effects of organophosphate pesticides in man. Clin. Toxicol. 9:391-405, 1976.

20. Li, C. Introduction to Experimental Statistics. New York: McGraw-Hill, 1964, p. 425.

21. Lindquist, E. Design and Analysis of Experiments in Psychology and Education. Boston: Houghton-Mifflin, 1953, pp. 56, 269.

22. Meeter, E. The mode of action of cholinesterase inhibitors on the temperature regulation of the rat. Arch. Int. Pharmacol. Ther. 182:416-419, 1970.

23. Meeter, E. and O. L. Wolthuis. The effects of cholinesterase inhibitors on the body temperature of the rat. Eur. J. Pharmacol. 4:18-24, 1968.

24. Mendoza, C. E. and J. B. Shields. Effects of hexachlorobenzene on malathion LD50 and on cholinesterase and carboxylesterase activities in organs of the suckling albino rat. Toxicol. Appl. Pharmacol. 35:447-453, 1973.

25. Namba, T., C. T. Nolte, J. Jackrel, and D. Grob. Poisoning due to organophosphate insecticides. Am. J. Med. 50:475-492, 1971.

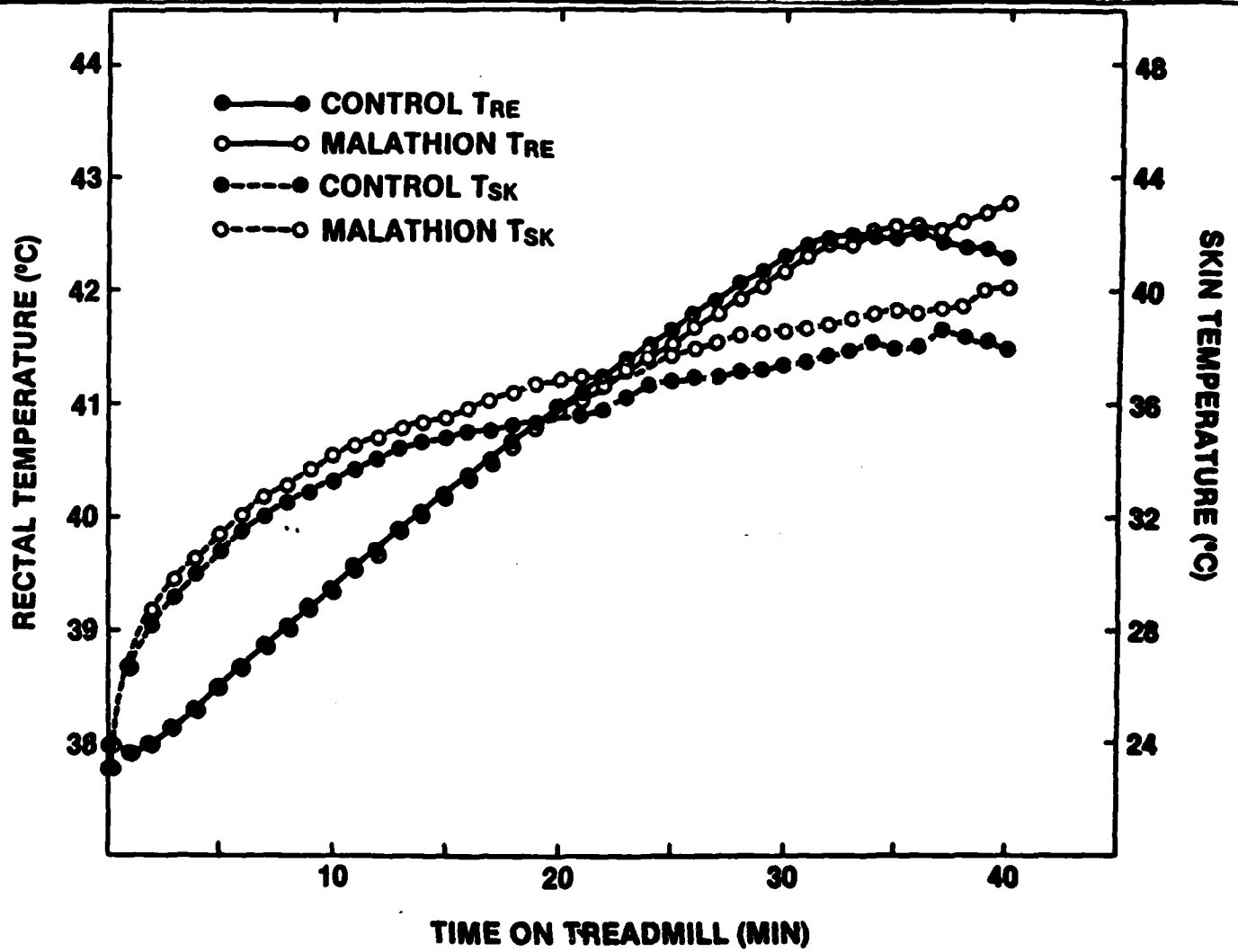
26. Paul, B. S., R. C. Gupta, and J. K. Malik. Influence of phenobarbitone and atropine on malathion induced toxicity and related biochemical changes in rats. Ind. J. Exp. Biol. 17:1096-1099, 1979.

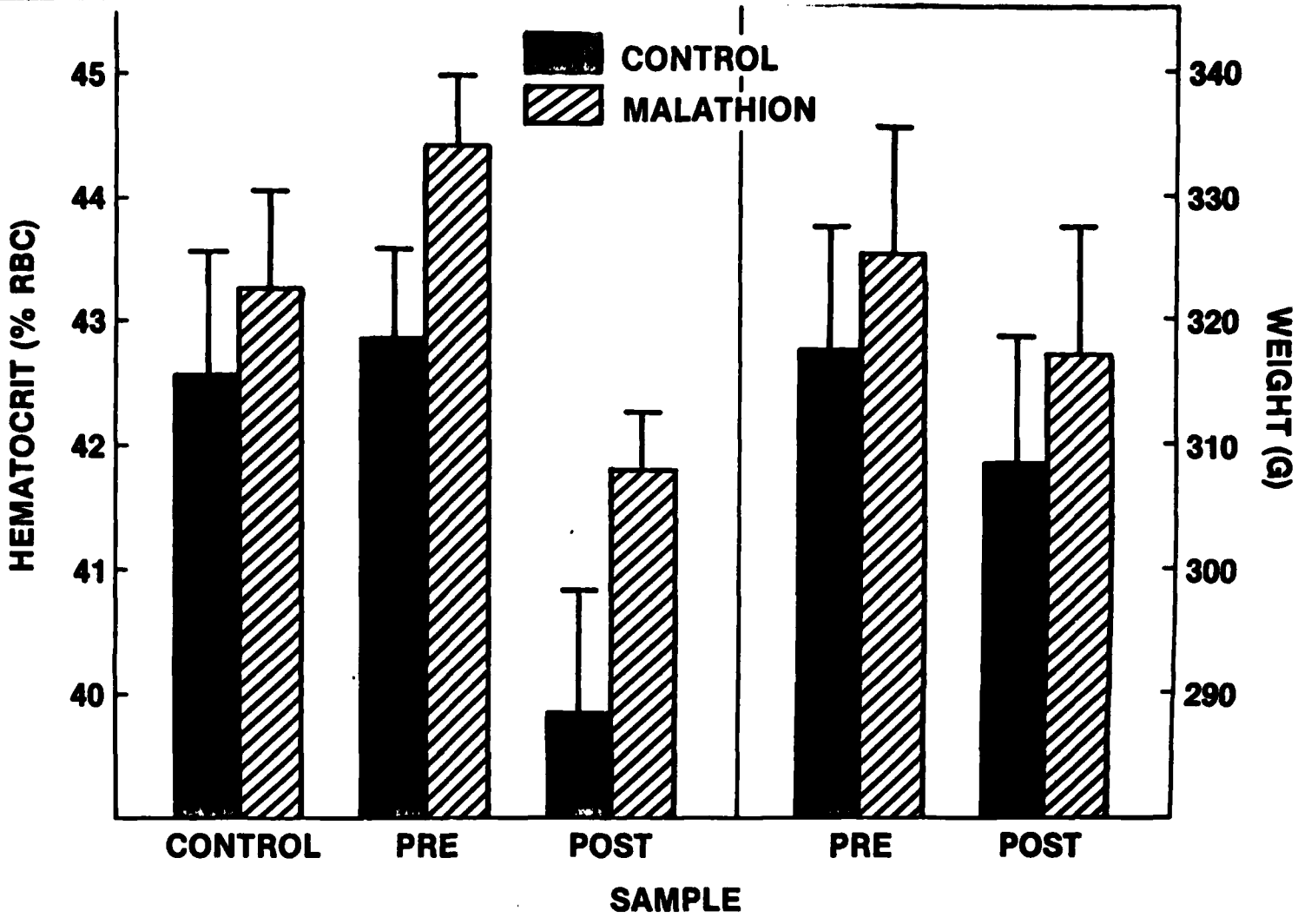
27. Perron, R. and B. B. Johnson. Insecticide poisoning. New Engl. J. Med. 281:274-275, 1969.

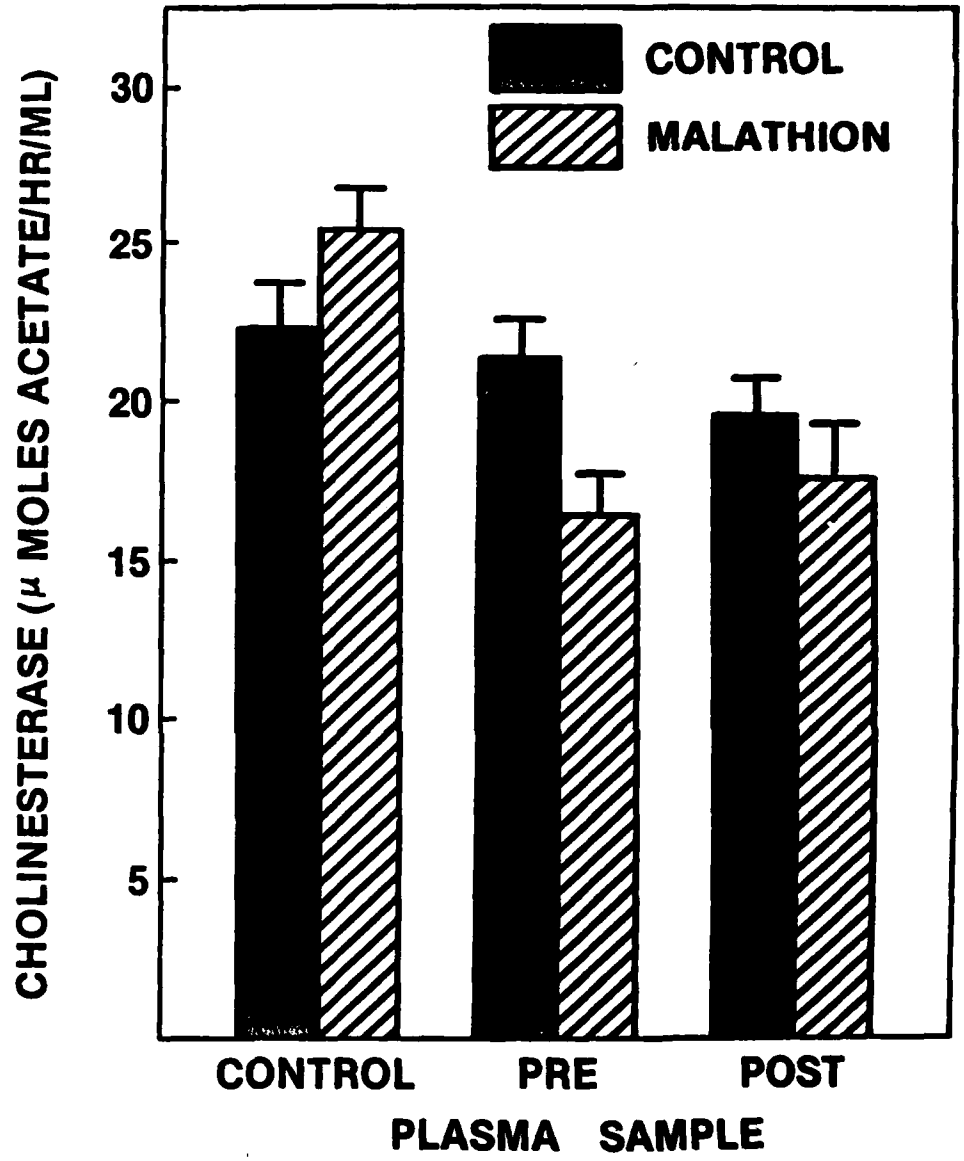
28. Sidell, F. R. Soman and sarin: clinical manifestations and treatment of accidental poisoning by organophosphates. Clin. Toxicol. 7:1-17, 1974.

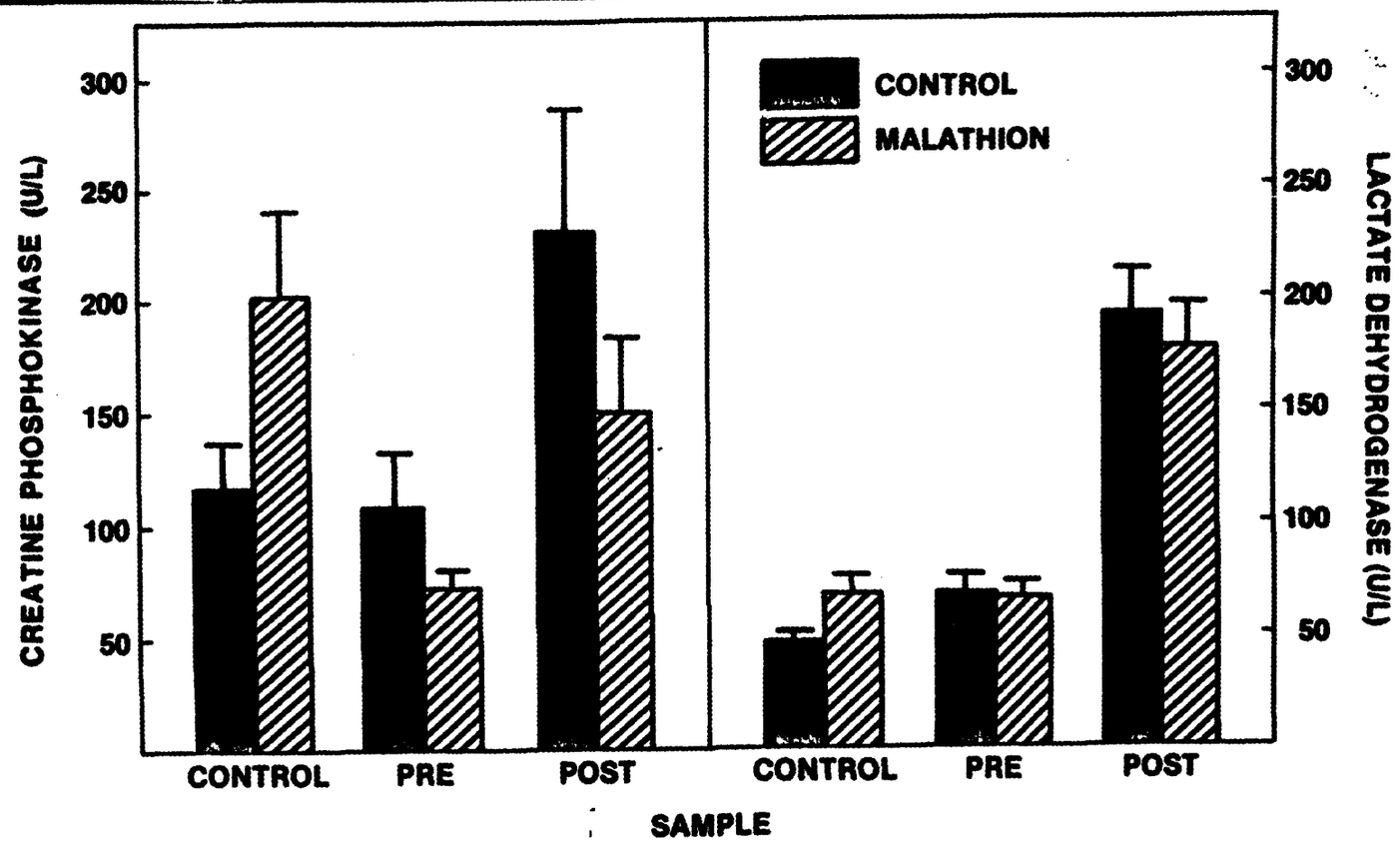
29. Townsend, B. A. and G. P. Carlson. Effect of halogenated benzenes on the toxicity and metabolism of malathion, malaoxon, parathion, and paraoxon in mice. Toxicol. Appl. Pharmacol. 60:52-61, 1981.

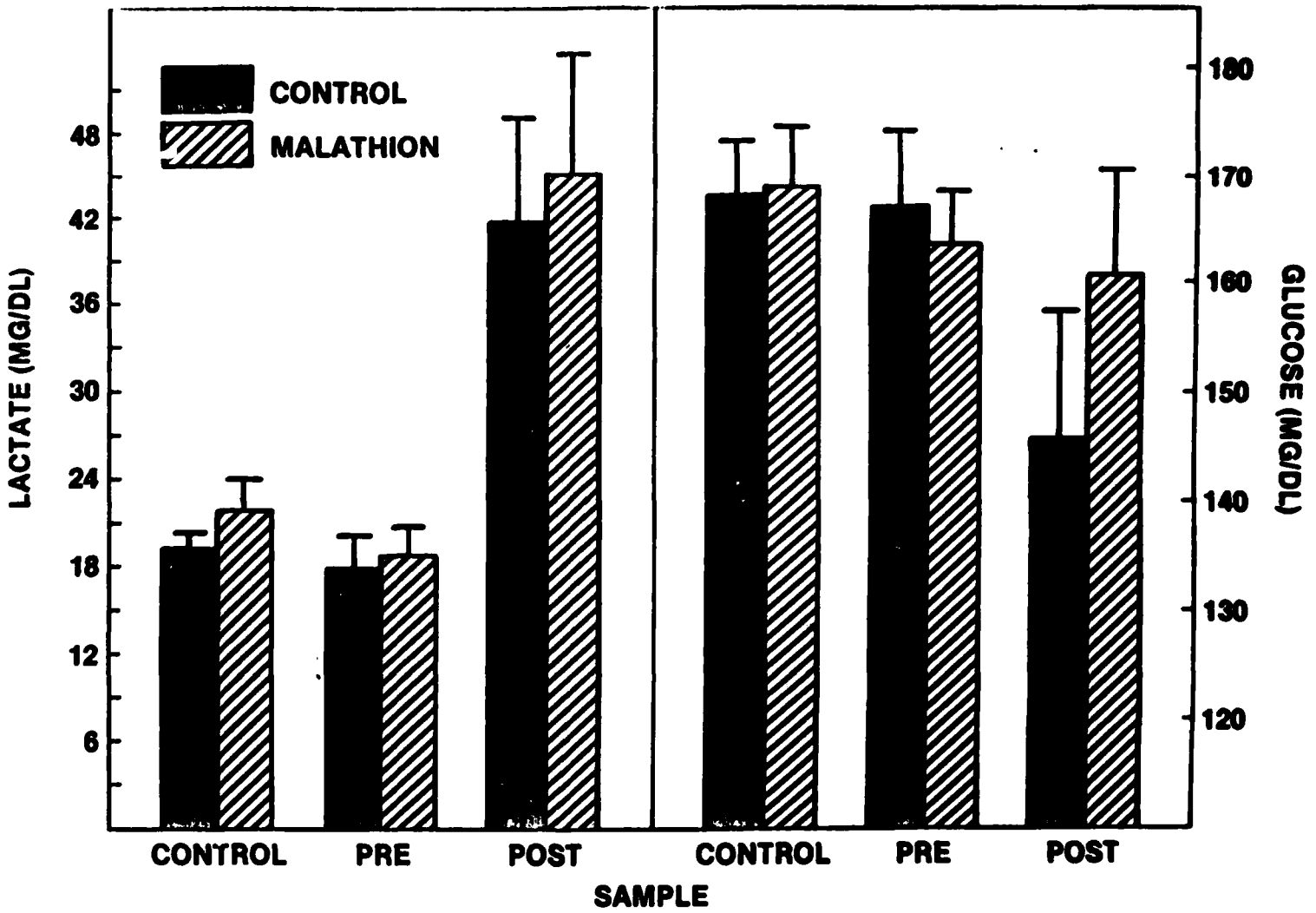
30. Villeneuve, D. C., M. J. van Logten, E. M. den Tonkelaar, A. G. Rauws, R. Kroes, and G. J. van Esch. The combined effect of food restriction and parathion exposure in rats. Arch. Environ. Contam. Toxicol. 7:37-45, 1978.

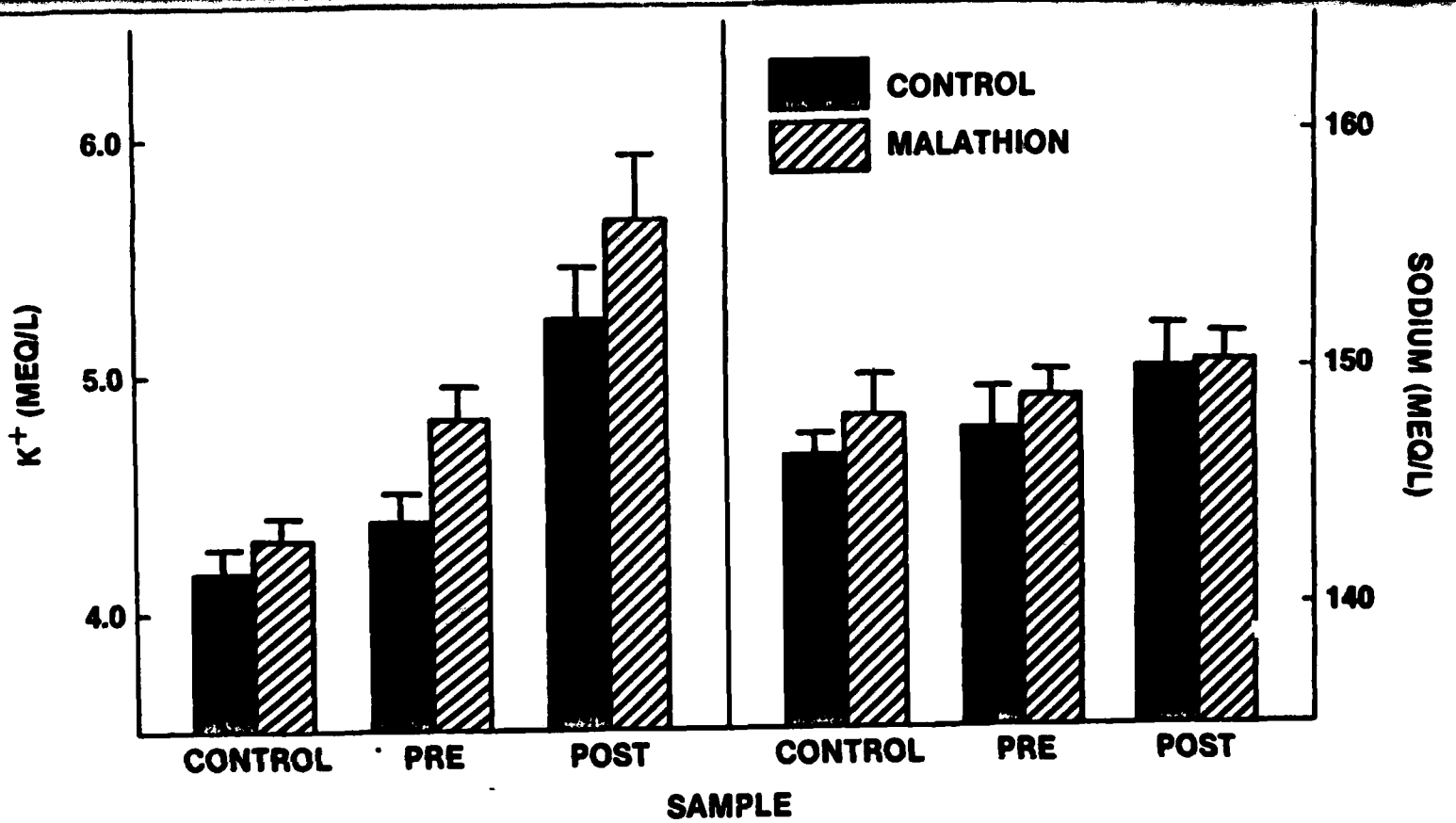

CONTROL T_{RE}
MALATHION T_{RE}
CONTROL T_{SK}
MALATHION T_{SK}
RECTAL TEMPERATURE (°C)
SKIN TEMPERATURE (°C)
TIME ON TREADMILL (MIN)
44
43
42
41
40
39
38
48
44
40
36
32
28
24
10
20
30
40


CONTROL
MALATHION
HEMATOCRIT (% RBC)
WEIGHT (G)
45
44
43
42
41
40
340
330
320
310
300
290
CONTROL
PRE
POST
PRE
POST
SAMPLE


CONTROL
MALATHION
CHOLINESTERASE (μ MOLES ACETATE/HR/ML)
30
25
20
15
10
5
CONTROL
PRE
POST
PLASMA SAMPLE


CREATINE PHOSPHOKINASE (U/L)
LACTATE DEHYDROGENASE (U/L)
300
250
200
150
100
50
CONTROL
MALATHION
CONTROL
PRE
POST
CONTROL
PRE
POST
SAMPLE


CONTROL
MALATHION
LACTATE (MG/DL)
48
42
36
30
24
18
12
6
180
170
160
150
140
130
120
GLUCOSE (MG/DL)
CONTROL
PRE
POST
CONTROL
PRE
POST
SAMPLE


CONTROL
MALATHION
6.0
5.0
4.0
K^+ (MEQ/L)
160
150
140
SODIUM (MEQ/L)
CONTROL
PRE
POST
CONTROL
PRE
POST
SAMPLE